CLAIMS

We claim:

~~1.~~ A variant protein comprising an Fc variant of a wild-type Fc polypeptide, said Fc variant comprising at least one amino acid modification in the Fc region of said wild-type Fc polypeptide, wherein said variant protein exhibits altered binding to an FcγR as compared to the wild-type Fc polypeptide.

2. A variant protein according to claim 1, wherein said Fc variant comprises at least one substitution at a position corresponding to an Fc position selected from the group consisting of: 230, 240, 244, 245, 247, 262, 263, 266, 273, 275, 299, 302, 313, 323, 325, 328, and 332.

3. A variant protein according to claim 1 wherein said altered binding is an increase in affinity of said Fc variant to said FcγR.

4. A variant protein according to claim 3, wherein said Fc variant binds with greater affinity to a mouse FcγR.

5. A variant protein according to claim 3, wherein said said FcγR is a human Fc receptor selected from the group consisting of FcγRI, FcγRIIa, FcγRIIb, FcγRIIc, and FcγRIIIa.

6. A variant protein according to claim 3, wherein said Fc variant binds with greater affinity to human FcγRI and FcγRIIIa, but exhibits unaltered affinity to a human receptor selected from the group consisting of FcγRIIa, FcγRIIb, and FcγRIIc.

7. A variant protein according to claim 6, wherein said Fc variant exhibits unaltered affinity to FcγRIIa, FcγRIIb, and FcγRIIc.

8. A variant protein according to claim 3, wherein the affinity increase for binding to one or more human FcγRII's is greater than the affinity increase for binding to human FcγRI and FγRIIIa.

9. A variant protein according to claim 3, wherein the affinity increase is the same for binding to FcγRIIa, FcγRIIb, and FcγRIIc.

10. A variant protein according to claim 9, wherein the affinity increase for binding to FcγRIIc is greater than the affinity increase for binding to FcγRIIb.

11. A variant protein according to claim 3, wherein said Fc variant binds with greater affinity to human FcγRIIa, but exhibits unaltered affinity to a human receptor selected from the group consisting of FcγRI, FcγRIIb, FcγRIIc, and FγRIIIa.

12. A variant protein according to claim 11, wherein saif Fc variant exhibits unaltered affinity to FcγRI, FcγRIIb, FcγRIIc, and FγRIIIa.

13. A variant protein according to any of claims 1-12, wherein said Fc variant binds with greater affinity to FcRn.

14. A variant protein according to any of claims 1-12, wherein said Fc variant binds with unaltered affinity to FcRn.

15. A variant protein according to any of claims 1-12, wherein said Fc variant binds with reduced affinity to FcRn.
16. A variant protein according to any of claims 1-12, wherein said Fc variant binds with greater affinity to C1q.
17. A variant protein according to any of claims 1-12, wherein said Fc variant binds with unaltered affinity to C1q.
18. A variant protein according to claim 1wherein said Fc variant further comprises an engineered glycoform.
19. A variant protein according to claim 18 wherein said engineered glycoform comprises an altered level of fucosylation or bisecting oligosaccharides as compared to the parent Fc polypeptide.
20. A variant protein according to claim 18 wherein said engineered glycoform improves effector function.
21. A variant protein comprising an Fc variant of a wild-type Fc polypeptide, said Fc variant comprising at least one amino acid modification in the Fc region of said wild-type Fc polypeptide, wherein said Fc variant modulates effector function as compared to the parent Fc polypeptide.
22. A variant protein according to claim 21, wherein said effector function is ADCC.
23. A variant protein according to claim 22, wherein said Fc variant improves ADCC in the presence of human effector cells as compared to said wild-type Fc polypeptide.
24. A variant protein according to claim 2 wherein said ADCC improvement is an enhancement in potency such that the EC50 of said Fc variant is approximately 5-fold greater than that of said parent Fc polypeptide.
25. A variant protein according to claim 23 wherein said ADCC improvement is an enhancement in potency such that the EC50 of said Fc variant is between approximately 5-fold and 1000-fold greater than that of said parent Fc polypeptide.
26. A variant protein according to claim 23 wherein said ADCC improvement is an enhancement in efficacy such that the maximal ADCC is approximately 2-fold greater than that of said parent Fc polypeptide.
27. A variant protein according to claim 26 wherein said Fc variant improves ADCC in the presence of mouse effector cells as compared to said wild-type Fc polypeptide.
28. A variant protein according to claim 21 wherein said effector function is ADCP.
29. A variant protein according to claim 28 wherein said Fc variant improves ADCP as compared to said wild-type Fc polypeptide.
30. A variant protein according to claim 25 or 29 wherein CDC is unaffected.
31. A variant protein according to claim 25 or 29 wherein CDC is ablated.

32. A variant protein according to claim 1 that has specificity for a target antigen selected from the group consisting of CD20, CD22, CD33, CD52, Her2/neu, EGFR, EpCAM, MUC1, GD3, CEA, CA 125, HLA-DR, TNFalpha, and VEGF.

33. A variant protein according to claim 1 or 21 comprising a modification selected from the group consisting of 239D, 239E, 239N, 239Q, 239T, 240I, 240M, 264I, 264T, 264Y, 297D, 330I, 330L, 330Y, 332D, 332E, 332N, 332Q, A231E, A231G, A231K, A231P, A231Y, A298H, A327D, A327E, A327F, A327H, A327I, A327K, A327L, A327M, A327N, A327P, A327R, A327T, A327T, A327V, A327W, A327Y, A330E, A330F, A330F, A330G, A330H, A330I, A330L, A330L/I332E, A330M, A330N, A330P, A330R, A330S, A330T, A330V, A330W, A330Y, A330Y, A330Y/I332E, D221K, D221Y, D249H, D249Q, D249Y, D265F, D265F/N297E/I332E, D265G, D265H, D265I, D265K, D265L, D265M, D265N, D265P, D265Q, D265R, D265S, D265T, D265V, D265W, D265Y, D265Y/N297D/I332E, D265Y/N297D/T299L/I332E, D270F, D270G, D270H, D270I, D270L, D270M, D270P, D270Q, D270R, D270S, D270T, D270W, D270Y, D280G, D280H, D280K, D280L, D280P, D280Q, D280W, D280Y, E233A, E233D, E233F, E233G, E233H, E233I, E233K, E233L, E233M, E233N, E233Q, E233R, E233S, E233T, E233V, E233W, E233Y, E258H, E258S, E258Y, E269F, E269G, E269H, E269I, E269K, E269L, E269M, E269N, E269P, E269R, E269S, E269T, E269V, E269W, E269Y, E272D, E272F, E272G, E272H, E272I, E272K, E272L, E272M, E272P, E272R, E272S, E272T, E272V, E272W, E272Y, E283G, E283H, E283K, E283L, E283P, E283R, E283Y, E293F, E293G, E293H, E293I, E293L, E293M, E293N, E293P, E293R, E293S, E293T, E293V, E293W, E293Y, E294F, E294G, E294H, E294I, E294K, E294L, E294M, E294N, E294P, E294R, E294S, E294T, E294V, E294W, E294Y, E318H, E318L, E318Q, E318R, E318Y, E333A, E333F, E333H, E333I, E333L, E333M, E333P, E333S, E333T, E333Y, E333Y, F241D, F241E, F241E/F243Q/V262T/V264E, F241E/F243Q/V262T/V264E/I332E, F241E/F243R/V262E/V264R, F241E/F243R/V262E/V264R/I332E, F241E/F243Y/V262T/V264R, F241E/F243Y/V262T/V264R/I332E, F241L, F241L/F243L/V262I/V264I, F241L/V262I, F241R, F241R/F243Q/V262T/V264R, F241R/F243Q/V262T/V264R/I332E, F241W, F241W/F243W, F241W/F243W/V262A/V264A, F241Y, F241Y/F243Y/V262T/V264T, F241Y/F243Y/V262T/V264T/N297D/I332E, F243E, F243L, F243L/V262I/V264W, F243L/V264I, F243Q, F243R, F243W, F243W, F243Y, F275L, F275W, F275W, G236A, G236D, G236E, G236F, G236H, G236I, G236K, G236L, G236M, G236N, G236P, G236Q, G236R, G236S, G236T, G236V, G236W, G236Y, G237D, G237E, G237F, G237H, G237I, G237K, G237L, G237M, G237N, G237P, G237Q, G237R, G237S, G237T, G237V, G237W, G237Y, G281D, G281K, G281P, G281Y, H224E, H224Y, H268D, H268E, H268F, H268G, H268I, H268K, H268L, H268M, H268P, H268Q, H268R, H268T, H268V, H268W, H285D, H285E, H285K, H285Q, H285W, H285Y, I332A, I332D, I332E, I332F, I332G, I332H, I332K, I332L, I332M, I332N, I332N, I332P, I332Q, I332R, I332S, I332T, I332V, I332W, I332Y, I332Y,

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34. A variant protein according to claim 1 or 21 wherein said variant protein is an antibody comprising said Fc variant.

35. A variant protein according to claim 1 or 21 wherein said variant protein is an Fc fusion protein comprising said Fc variant.

36. A pharmaceutical composition comprising a variant protein according to claim 1 and a pharmaceutically acceptable carrier.

37. A method of treating a mammal in need of said treatment, comprising administering a variant protein of claim 1.